MAIL ROOM
NOV 19 1990
PAT. & TRADEMARK OFF.

Loc 030 A/N

WP+ 289U 030 11-13 CRP-056 11/12/90

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|---|---|---|---|
| Applicant: | Oppermann et al. | Examiner: | |
| Serial No.: | 599,543 | Group Art Unit: | |
| Filed: | October 18, 1990 | Attorney Docket: | CRP-056 |
| Title: | OSTEOGENIC DEVICES | | |

Honorable Commissioner of Patents and Trademarks
Washington, DC 20231

**********

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Honorable Commissioner of Patents and Trademarks, Washington, DC 20231 on the date set forth below.

11/16/90
Date of Signature
and of Mail Deposit

By _____
Edmund R. Pitcher
Registration No. 27,829
Attorney for Applicants

**********

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their attorney are aware of the following publications and information, and in accordance with 37 CFR 1.97, hereby make a record of those publications which have been identified in, or reviewed during the preparation of this application. A PTO Form 1449, listing each publication made of record is enclosed. The pertinence of each publication listed as presently understood is described below.

NOV 21 1990

We enclose copies of Sedivy (1988) and Bendig (1988). All of the other documents have been submitted for the parent case from which this case depends (USSN 179,406, filed April 8, 1988, now US Patent No. 4,968,950), as well as for previously filed related cases (see for example, USSN 232,630, filed April 15, 1988; USSN 315,342 filed February 23, 1989; and USSN 422,613, filed October 17, 1989) and have been duly recorded by the Examiner in each case. Accordingly, with the Examiner's permission (granted in a telephone conversation with Examiner Nutter on September 25, 1990), copies of these documents are not enclosed as they are already of record and are in the Examiner's hands.

U.S. 4,172,128 is understood to disclose a method for degrading and regenerating bone and tooth material by converting demineralized natural bone or tooth material to a mucopolysaccharide-free colloidal solution, adding a physiologically inert foreign mucopolysaccharide, and gelling and remineralizing the solution.

U.S. 4,294,753 is understood to relate to the process of separating bone morphogenetic protein from demineralized bone tissue.

U.S. 4,394,370 is understood to relate to an osteogenic collagen conjugate material, particularly in the form of a sponge, and to a process for making this material. The material is comprised primarily of reconstituted collagen.

U.S. 4,434,094 is understood to relate to partially purified osteogenic factor and to a process for preparing it from demineralized bone.

U.S. 4,455,256 is understood to relate to the characterization of bone morphogenic protein prepared from demineralized bone.

U.S. 4,563,350 is understood to disclose a composition suitable for inductive bone implants comprising a carrier having a percentage of non-fibrillar collagen.

U.S. 4,563,489 understood to relate to a polylactic acid polymer delivery system for bone morphogenic protein.

U.S. 4,657,548 is understood to disclose a delivery system for implantation of fine particles in surgical procedures, comprising a collagen tube made of a cast collagen film.

U.S. 4,703,108 is understood to disclose a biodegradable matrix comprising artificially cross-linked collagen in sponge or sheet form.

U.S. 4,725,671 is understood to disclose an atelopeptide non-fibrillar collagen fiber network for use in cell cultivation.

U.S. 4,789,663 is understood to disclose a method of bone repair comprising atelopeptide, artificially-crosslinked collagen.

U.S. 4,795,467 is understood to disclose a composition for bone repair comprising calcium phosphate minerals and atelopeptide, reconstituted, cross-linked, fibrillar collagen.

U.S. 4,812,120 is understood to disclose a prosthetic dental device having an outer layer in which collagen fibrils are embedded.

U.S. 4,824,939 is understood to disclose a leading process for separating extractable material from a particular solid useful in the recovery of gelatin from bone.

U.S. 4,837,285 is understood to disclose porous collagen matrix beads for soft tissue repair.

U.S. 4,877,864 is understood to claim an amino acid sequence isolated from bone (BMP-1) and a DNA sequence encoding it. This protein is purported to have osteogenic activity.

U.S. 4,894,441 is understood to disclose a process for extracting high parity collagen in the form of a viscous gel from bovine bone.

PCT/US89/09605 is understood to disclose a polypeptide sequence isolated from bone having osteogenic activity at non-bony sites in the presence of TGF-ß.

PCT/WO85/05274 is understood to disclose a collagenous fibrous tissue preparation for repair of cutaneous wounds and soft tissue injuries. The tissue preparation, preferably in sheet form, is produced by treatment of the tissue with a polyisocyanate.

PCT/WO86/00526 is understood to claim a method for treating implants to enhance or stimulate cartilage and/or bone formation.

PCT/WO88/00205 is understood to relate to the partial purification of bovine bone morphogenic factors from bone and to the identification of genetic sequences using probes derived from tryptic digests of the impure factor mix.

PCT/WO89/10409 is understood to disclose a polypeptide sequence isolated from bone (BMP-3), and a DNA sequence encoding it. The protein is purported to have osteogenic activity.

PCT/WO90/03733 is understood to describe the isolation and analysis of a family of osteogenic factors called "P3 0F 31-34." This protein family contains at least four proteins, which are characterized by peptide fragment sequences. Only the impure mixture P3 OF 31-34 is assayed for osteogenic activity.

EPO 069,260 is understood to disclose a collagen insert containing an active ingredient for introduction into bones or soft parts. The collagen insert comprises highly pure collagen sheets.

EPO 128,041 is understood to describe three polypeptide compositions exhibiting skeletal growth factor activity.

EP0 148,155 is understood to relate to a protein extracted from demineralized bone reportedly capable of promoting osteogenesis, and to a method for its isolation and purification. The matrix used in bone growth assays is prepared by conventional methods.

EPO 169,001 is understood to disclose a collagen-coated prosthesis comprising purified, atelopeptide collagen prepared from bone or skin.

EPO 169,016 is understood to disclose two polypeptide cofactors isolated from bone having chondrogenic and TGF-ß activity.

EP0 182,483 is understood to claim a composition suitable for inductive bone implants comprising non-fibrillar, atelopeptide collagen.

EPO 170,979 is understood to disclose a resorbable implant comprising reconstituted, crosslinked collagen tissue or sponge.

EP0 212,474 is understood to relate to the production and isolation of bone morphogenic peptide agents by recombinant means. The matrix used in bone growth assays is prepared by conventional methods.

EPO 230,647 is understood to disclose a method of preparing a sustained release vehicle comprising atelopeptide non-fibrillar collagen and/or gelatin.

EPO 309,241 is understood to claim a method of bone repair using an osteogenic matrix extract, and a matrix carrier of mineral particles and collagen.

GB 2 178 447 is understood to disclose a fibrous or porous foam matrix for in vitro cell cultivation.

Canalis et al. (1980) is understood to relate to the stimulation of DNA and collagen synthesis by a growth factor in cultured fetal rat calvariae.

Glowacki et al. (1981) is understood to relate to the application of demineralized bone implants for cranio-maxillofacial reconstruction involving osteogenesis.

Reddi (1981) is understood to relate to a review of the cell biology and biochemistry of endochondral bone development, including a discussion of the developmental cascade of bone resorption and remodeling.

Sampath et al. (1981) is understood to relate to the dissociative extraction and reconstitution of extracellular matrix components involved in local bone differentiation.

Farley et al. (1982) is understood to relate to human skeletal growth factor and to characterization of its mutogenic effect on bone cells in vitro.

Maugh (1982) is understood to announce the isolation of human skeletal growth factor and distinguishes it from bone morphogenic protein.

Sampath et al. (1983) is understood to relate to the bone inductive proteins from human, monkey, bovine, and rat extracellular matrix, and to a comparison of their biochemical and enzymatic characteristics.

Seyedin et al. (1983) is understood to describe an in vitro system developed to study the onset of chondrogenesis.

Urist et al. (1983) is understood to relate to the physical and biological characterization of several human bone morphogenetic proteins extracted from demineralized, gelatinized cortical bone matrix.

Simpson (1984) is understood to review the role of growth factors in both bone resorption and formation, as understood to date.

Strand et al. (1984) is understood to disclose a matrix for in vitro cell cultivation comprising microcarrier beads of DEAE or polyacrylamide.

Urist et al. (1984) is understood to relate to the differentiation of cartilage into bone by induction with an aggregate of ß-tricalcium phosphate and bone morphogenetic protein.

Urist et al., II (1984) is understood to relate to the purification and characterization of several bovine bone morphogenetic proteins by hydroxyapatite chromatography.

Centrella et al. (1985) is understood to relate to the purification and characterization of transforming and nontransforming growth factors present in medium conditioned by fetal rat calvariae.

Klausner (1985) is understood to relate to the isolation of two cartilage-inducing factors, and to an in vitro assay for chondrogenetic activity.

Olson et al. (1985) is understood to describe the deglycosylation of chondroitin sulfate proteoglycan with hydrogen fluoride in pyridine.

Reddi (1985) is understood to relate to the cascade of implant-stimulated interface reactions which occur during collagenous bone matrix-induced bone formation.

Sampath et al. (1985) is understood to relate to a review of the cellular and biochemical events associated with matrix-induced endochondral bone formation, and to the role of extracellular matrix components in these events.

Seyedin et al. (1985) is understood to relate to the purification of two cartilage-inducing factors from bovine demineralized bone including dissociative extraction, gel filtration, cation exchange chromatography, and reverse phase HPLC. It also is understood to relate to the characterization of these cartilage-inducing factors.

Colowick et al. (1987) is understood to describe a method of preparing bone morphogenic protein and polypeptide fragments.

Deatherage et al. (1987) is understood to describe a delivery system for bone induction factors comprising purified, non-fibrillar human Type-I collagen.

Padgett et al. (1987) is understood to disclose the cDNA sequence of a drosophila development gene (DPP-C) and indicates its homology to the related genes of the TGF-ß gene family.

Sampath et al. (1987) is understood to relate to the isolation and characterization of an extracellular, matrix-associated bone inductive protein by heparin affinity chromatography.

Spector (1987) is understood to review the state of the art of porous-coated implants as understood to date.

Weeks et al. (1987) is understood to relate to the characterization and localization of a maternal mRNA from Xenopus eggs which encodes a member of the transforming growth factor-B family of proteins (Vg-1).

Aspenberg et al. (1988) is understood to describe experiments done on bone induction in adult monkeys.

Bendig (1988) is understood to review the current methods and technology for mammalian cell expression systems, as understood to date.

Cook et al. (1988) is understood to evaluate hydroxyapatite-coated titanium for use in orthopedic implant applications.

Deatherage et al. (1988) is understood to review matrix-induced osteogenesis as understood to date, with specific reference to its use in cranio-facial surgery.

LeGendre et al. (1988) is understood to relate to the use of Immobilon transfer membranes on to which proteins have been electrophoretically transferred for direct protein sequencing in a gas phase sequencer.

Sedivy (1988) is understood to review new genetic methods for mammalian cells and, in particular, to describe a method of gene amplification using temperature-sensitive BSC-40 cells (BSC-40tsA-58), from a cultured monkey kidney cell line.

Wang et al. (1988) is understood to relate to the isolation and characterization of factors from bovine bone that induce cartilage and ectopic bone formation in vivo.

Wang et al., II (1988) is understood to relate to the isolation and characterization of factors from demineralized bone that induce cartilage and new bone formation in vivo.

Wozney et al. (1988) is understood to relate to the cloning and identification of three proteins involved in in vivo cartilage formation.

Wozney et al., II (1988) is understood to relate to the cloning and identification of three proteins involved in in vivo cartilage formation.

Lyons et al. (1989) is understood to relate to a sequence comparison of Vgr-1 DNA with that of other DNA sequences corresponding to proteins thought to be in the TGF-ß superfamily.

Wang et al. (1990) is understood to describe the expression and partial purification of one of the cDNA sequences described in WO88/00205. Consistent cartilage and/or bone formation with this composition requires 600 ng of 50% pure material.

Respectfully submitted,

LAHIVE & COCKFIELD

Edmund R. Pitcher
Attorney for Applicants
Reg. No. 27,829

60 State Street
Boston, MA 02109
(617) 227-7400
Date: